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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/460,216	12/13/1999	GRAHAM P. ALLAWAY	50875-F-PCT-	2202

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/460,216	ALLAWAY, G. P. ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 22 October, 2004. Claim 61 is pending and claims 1-60 and 62-65 have been canceled without prejudice or disclaimer.

37 C.F.R. § 1.98

The information disclosure statement filed 22 October, 2004, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claim 61 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claim is directed toward a method of inhibiting HIV-1 macrophage-tropic infection of a $CD4^+$ cell by contacting said cell with an agent that is capable of binding to cell surface CCR5. The claim also stipulates that said agent blocks HIV-1_{JR-FL} fusion with a PM-1

cell while not affecting fusion of the HIV-1_{BRU} with the same cell type.

As previously set forth, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had **possession** of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of **agents** that are capable of abrogating HIV-1 infection by binding to the CCR5 chemokine receptor. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, **structures**, figures, diagrams, and **formulas** that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). **The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest.** *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). **The court**

noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or **structural chemical formulas** that are sufficiently detailed to show that applicant was in **possession** of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., **complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.** For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, **chemical structure**, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or

disclosed correlation between structure and function, and the method of making the claimed invention.

The claim of the instant application is broadly directed toward **any agent** that is capable of abrogating HIV-1 infection through CCR5 binding interactions. The claims do not limit the genus to any particular type of compound (i.e., peptidyl, organic, fatty acid, etc.) or any particular family of compounds (small molecular weight peptidyl inhibitors, antibody-based reagents, etc.). The disclosure provides a generic *in vitro* resonance energy transfer (RET) screening assay that enables the skilled artisan to detect HIV-1 fusion events. This method by itself does not lead the skilled artisan to any particular class of compounds. The disclosure also fails to provide sufficient structural/functional guidance pertaining to suitable compounds that can reasonably be expected to function in the claimed methodology. While some data is supplied pertaining to a small number of closely related molecules (e.g., the β-chemokines), nevertheless, these compounds fail to meet the basic limitations of the claim pertaining to fusion blocking acivity. Furthermore, the disclosure fails to provide any guidance pertaining to the molecular determinants of the CCR5 receptor that might prove as suitable targets (i.e., epitopes, active domains, etc.). Thus, the skilled artisan cannot perform a rational drug-screening approach to identify putative inhibitors. Basically, applicants have provided a generic screening method and invited the skilled artisan to figure out which agents may be reasonably expected to function in the recited manner. This clearly fails to meet the requirements set forth under this statute. Accordingly, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed genus of compounds at the time of filing.

Response to Arguments

Applicants traverse and submit that sufficient written support for the claimed invention is clearly present in the specification

and rely upon different passages therein (i.e., pages 34 and 35). The examiner does not concur with this assessment. Perusal of the portions relied upon fails to provide adequate written support for the large genus of agents. The only molecules described with any detail are a small number of structurally related compounds, the β-chemokines, that are ligands for the CCR5 receptor. Perusal of the data pertaining to these compounds illustrates that most of the compounds referenced fail to meet the basic claim limitations. The claims require that the agent of interest needs to block fusion of the JR-FL isolate without blocking fusion of the BRU isolate. A review of the compounds tested indicates that there was considerable variability in the ability of any given compound to block JR-FL-mediated fusion. For example, compounds MIP-1α, MIP-1β, MCP-1, -2, and -3 inhibited fusion 61%, 87%, 1%, 28%, and 2%, respectively. Fusion inhibitory rates for these same compounds in the context of BRU-mediated fusion were 0%, 7%, 2%, 7%, and 1%, respectively. Thus, very few of the compounds appear to be able to truly block JR-FL-mediated Env fusion events without also inhibiting BRU-mediated Env fusion events. Moreover, the rates of inhibition varied considerably even amongst closely related compounds. Thus, this example fails to provide sufficient structural information that would put applicants in possession of the genus of agents.

Applicants further contend that the disclosure provides sufficient means for performing rational drug-screening strategies. The skilled artisan would clearly disagree with this statement. Rational drug-screening strategies generally rely upon detailed structural determinations of the target (which are frequently obtained from x-ray crystallographic models) in conjunction with the chemical synthesis of compounds that might be expected to bind in a specific manner to a specific portion of the target. The disclosure fails to provide any detailed structural information pertaining to the molecular determinants of CCR5 that should be targeted. Applicants are invited to identify those domains and the

corresponding amino acid regions that should be targeted by a rational drug-screening regimen. Absent such a showing the rejection is clearly tenable.

Finally, applicants argue that the examiner has ignored the evidence provided by Dr. Dragic in the form of two declarations. This evidence was considered and clearly found to be non-persuasive for the reasons of record. The declaration dated 08 April, 2002, asserted that the skilled artisan could use the disclosed FRET assay to identify suitable agents. Reference was made to a recently published abstract. It should be noted that the abstract failed to set forth any meaningful structural information pertaining to the compounds that were identified. Dr. Dragic also asserted that p. 45 of the specification disclosed a compound that meets the claimed limitations, specifically JM-3100. Perusal of the disclosure at pages 45 and 46 clearly demonstrated that JM-3100 did **not** inhibit JR-FL Env-mediated fusion as required by the claim. In fact, the inventors unambiguously stated that this product binds to CXCR4, not CCR5. Thus Dr. Dragic's comments are clearly erroneous. This declaration failed to provide any evidence that would put applicants in possession of a sufficient number of compounds that would provide a sufficient written description for the claimed genus.

Concerning the second declaration dated 29 August, 2003, Dr. Dragic referenced the following in support of her arguments: 1) a post-filing data PCT publication provided putative compounds that meet the claimed limitations; 2) the earlier referenced abstract was again cited; 3) Data from PROGENICS in-house experiments involving SCH-C, TAK-779, 7948, and 8260 was provided; and 4) data from a single Mab (e.g., PRO-140) was provided. First, it should be noted that none of the evidence relied upon directly suggests that applicants were in possession of any of the claimed compounds at the time of filing. Dr. Dragic's declaration clearly fails to state that the inventors had synthesized and identified any of these compounds at the time of filing. Second, much of the data

surrounding the inhibitory activity of these compounds is incomplete. For instance, SCH-C inhibitory values were reported for JR-FL isolates but not BRU. Thus, a direct and meaningful comparison does not appear to have been performed. Third, the fact that others may have identified a limited number of compounds that may meet the claim limitations, does not put them in applicants' possession at the time of filing. The crux of the rejection is not whether or not one skilled in the art could use the disclosed FRET assay to identify putative antivirals, but whether or not applicants had already used said assay to identify a reasonable number of compounds that would justify the breadth of the claim language directed toward any agent. The skilled artisan upon considering the teachings of the disclosure would reasonably conclude that applicants were clearly not in possession of the claimed compounds at the time of filing.

Finality of Office Action

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from

10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

05 February, 2005